[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Benzocycloöctanone-3

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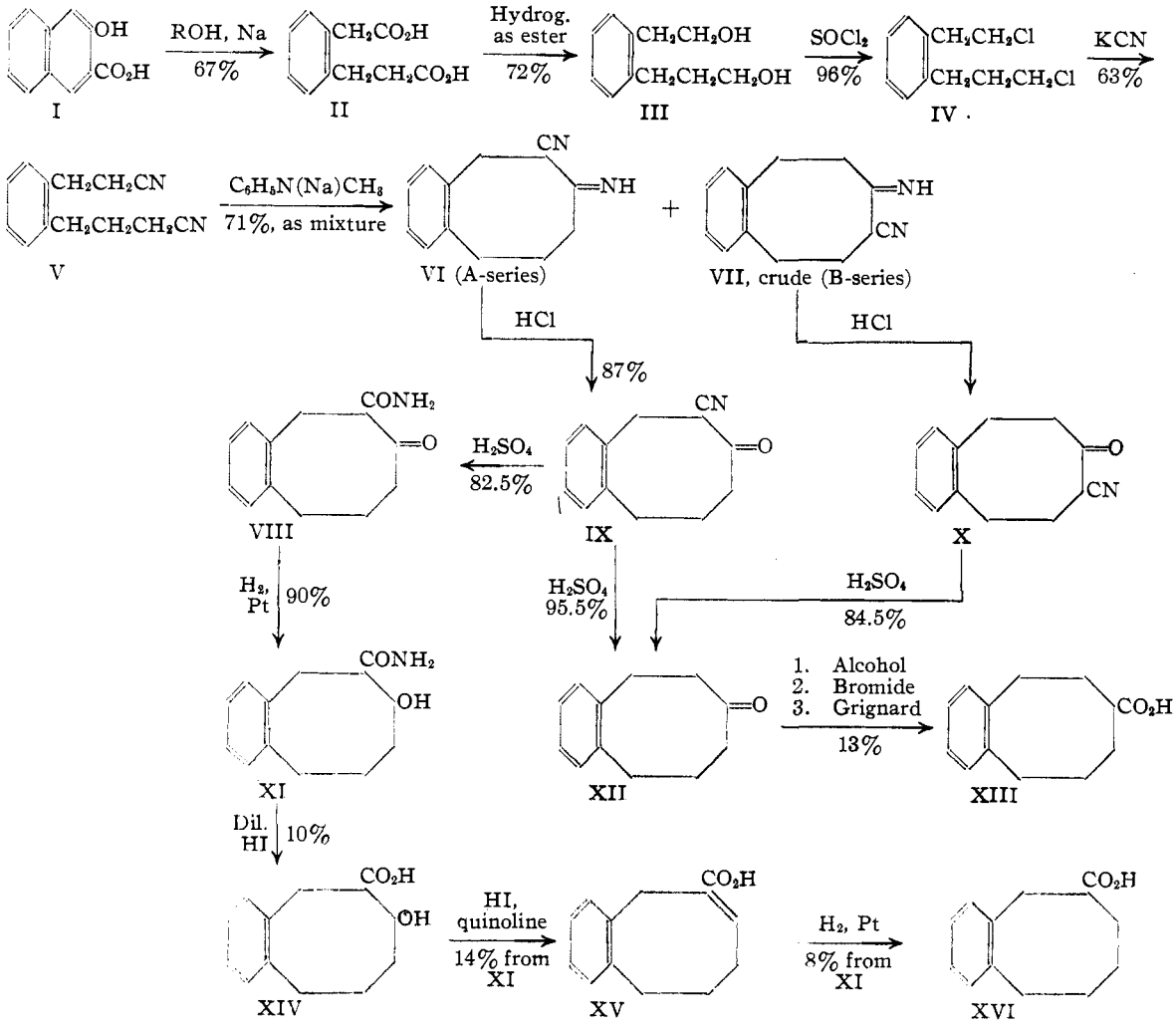
Wawzonek,[2] in a recent paper, calls attention to the possibility of gaining useful information on the nature of the cycloöctatetraene ring system by the study of benzo derivatives of the parent hydrocarbon. Substances in this group may well prove to be both more readily accessible and more stable than cycloöctatetraene itself. Wawzonek developed an ingenious approach to certain *sym*-dibenzocycloöctatetraenes, but encountered obstacles in the terminal stages of the synthesis which were not overcome. The present work, which was in progress at the time of the appearance of Wawzonek's paper, represents an initial step toward the development of a synthesis of benzocycloöctatetraene.

One possible method of fusing a side ring of the desired carbon content to the benzene nucleus would consist in the cyclization of ϵ-phenylcaproic acid, but as preliminary trials with both the acid and the acid chloride were unpromising this route was abandoned. We next sought to utilize the excellent method elaborated by Ziegler[3] for the cyclization of long-chain dinitriles. A suitable starting point was found in the novel reductive cleavage reaction of Einhorn and Lumsden.[4] Their procedure for the reduction of 2-hydroxy-3-naphthoic acid (I) with sodium and amyl alcohol was found applicable on a large scale, affording a ready source of *o*-phenylene acetic propionic acid (II). The corresponding ester was converted smoothly by high pressure hydrogenation over copper chromite catalyst to the dialcohol III, and this in turn could be transformed through the dichloride to the dinitrile V in good yield.

The cyclization of the dinitrile was carried out by Ziegler's method,[3] using methylaniline as the sodium carrier[5] and following the greatly simplified technique of Kohler and Schroeder.[6] Methylaniline was converted into the sodium derivative with the use of naphthalene[6] as the assistant, and the dinitrile solution was introduced slowly into the condensate of a vigorously refluxing and well stirred ethereal solution of the condensing agent. On addition of the reagent at a rate slow enough to provide reasonably high dilution the reaction proceeded smoothly and afforded a mixture of isomeric imino nitriles in good yield (71%), and the yield did not drop materially when the addition was conducted more rapidly. The condensation proceeds in two directions, giving a mixture of isomeric imino nitriles which will be referred to as belonging to the A- and B-series. The present work indicates that these substances probably have the structures VI and VII, respectively, and although the proof of structure is as yet incomplete these formulations will be employed in the following discussion. The A-isomer VI predominates in the reaction mixture and is the less soluble of the two imino nitriles and hence was easily isolated in quantity in a pure condition. Gentle acid hydrolysis afforded the keto nitrile IX, and this on more drastic treatment with acid was converted smoothly into benzocycloöctanone-3 (XII). In the B-series, although the imino nitrile was not secured in a pure state the keto nitrile X could be isolated after hydrolysis of the total imine mixture, and this afforded a ketone identical with that obtained from the A-isomer.

An attempt to establish the structures of the A and B compounds was based on the consideration that in benzocycloöctane the 3 and 4 positions (B) are identical while the 2 and 3 positions (A) are not. A reference substance was first produced by reducing benzocycloöctanone-3 to benzocycloöctanol-3 by high pressure hydrogenation, and transforming this in turn into the bromide, the Grignard derivative, and the acid, benzocycloöctane-3-carboxylic acid (XIII). The plan then was to operate on the two keto nitriles in such a way as to eliminate the oxygen and hydrolyze the nitrile group. The symmetrically substituted keto nitrile X should give the 3-acid XIII, while IX should yield the isomeric 2-acid XVI. The second transformation was realized by the sequence of reactions shown on the chart. Gentle acid hydrolysis gave the amide VIII, the ketone group of which was then reduced by catalytic hydrogenation. Mild treatment with

(1) Du Pont Research Fellow, 1938–1940.
(2) Wawzonek, THIS JOURNAL, **62**, 745 (1940).
(3) Ziegler, Eberle and Ohlinger, *Ann.*, **504**, 94 (1933).
(4) Einhorn and Lumsden, *ibid.*, **286**, 268 (1895).
(5) Ziegler and co-workers, *ibid.*, **511**, 64 (1934).
(6) H. E. Schroeder, Dissertation, Harvard University, 1938.



hydriodic acid produced the hydroxy acid XIV, while the more vigorous action of this reagent followed by treatment with quinoline resulted in the formation of an unsaturated acid. This on hydrogenation gave an acid melting at 80° and isomeric with the 3-acid XIII, m. p. 144°. From this comparison and from the method of synthesis it appears that the lower melting substance is benzocycloöctane-2-carboxylic acid (XVI). In the less accessible B-series the keto nitrile had been transformed only into keto amide and hydroxy amide at the time the investigation had to be interrupted.

Benzocycloöctanone-3 (XII) is a colorless, crystalline substance melting at 49–50°. The compound evaporates readily in the solid state and is volatile with steam. By the present eight-step synthesis the ketone can be produced in 17% over-all yield from an inexpensive starting material and it may provide a suitable intermediate for the synthesis of benzocycloöctatetraene. This possibility will be investigated.

Experimental Part[7]

o-Phenyleneaceticpropionic Acid[4] (II).—A 3-liter flask equipped with a reflux condenser, a thermometer, and a dropping funnel was charged with 110 cc. of *n*-amyl alcohol and 25 g. of sodium and heated in an air- or sand-bath until the temperature of the refluxing liquid reached 158°. A reaction temperature of 158–165° was then maintained by the suitable alternate addition of a solution of 50 g. of 2-hydroxy-3-naphthoic acid in 750 cc. of *n*-amyl alcohol and of 70 g. of sodium (in 5-g. chunks) in the course of one and one-half hours. A too rapid addition of the alcohol solution results in an undue drop in the temperature of the refluxing mixture, while a too high concentration of sodium derivative causes the separation of a hard cake at the bottom of the flask. The cake should be dislodged with a stirring rod as first formed, when it promptly dissolves.

(7) Microanalyses by Lyon Southworth. All melting points are corrected.

After the above reagents had been introduced the milky solution was maintained in reflux for one-half hour longer, during which time 20 g. more sodium and 390 cc. of amyl alcohol were added. Heating was then continued for one hour longer and the mixture, containing some unreacted sodium, was allowed to cool and to stand overnight. The heavy liquor was transferred to a large beaker and decomposed by the very cautious addition of 600 cc. of water.

At this point two simultaneous runs were conveniently combined. The red aqueous alkaline layer was separated from the reddish alcohol layer and the latter was further washed with about 1 liter of water in portions, acidified, dried by distillation, and recovered. The aqueous liquor was washed with ether to remove traces of amyl alcohol, partially neutralized with 500 cc. of concentrated hydrochloric acid, cooled, and transferred to a 5-liter separatory funnel. Cautious addition of more acid precipitated a red oil which was removed by ether extraction, and after repeating this process until the solution had been considerably clarified the *o*-phenylene acetic propionic acid was precipitated by full neutralization of the solution (about 500 cc. of acid). This afforded 57 g. of yellow crystalline solid, m. p. 140–143°, suitable for conversion to the ester. The combined ether extracts and washings yielded 17.2 g. of satisfactory product, m. p. 135–140°; total yield 67%.

The **diethyl ester** was prepared by suspending 40 g. of the acid in 220 cc. of absolute ethanol, passing in dry hydrogen chloride rapidly until the temperature rose to 60°, and allowing the resulting solution to stand at room temperature for forty-five minutes. After adding 30 g. of sodium carbonate, the alcohol was distilled under diminished pressure at 30–40° and the oily product was extracted with ether. Extraction with sodium bicarbonate solution removed 3.5 g. of partially esterified starting material. The ester was collected and distilled, giving 44.5 g. (96%) of material with b. p. 160–162° at 2 mm.

1-(β-Hydroxyethyl)-2-(γ-hydroxy-*n*-propyl)-benzene (III).—A glass bomb-liner was charged with 66.5 g. of the diester, 33 cc. of dioxane, and 10 g. of copper chromite catalyst 39KAF[8] and the mixture shaken with hydrogen at 185° and a pressure (hot) of 2400–2800 lb. The reaction was complete after about seventy-five hours. After removal of the catalyst and distillation of the solvent the oily product was refluxed for one-half hour with 100 cc. of 2 *N* sodium hydroxide to saponify any unreacted ester and the neutral fraction was recovered by ether extraction and distilled. After separation of 9.7 g. of a fore-run boiling below 167° (2 mm.) and probably containing products of over-hydrogenation, the dialcohol distilled at 169–175° (2 mm.) as a colorless, viscous oil weighing 34.1 g. (75%). There was no residue, and no acid was obtained on neutralization of the alkaline extract. The purified dialcohol boiled at 174.5–175.5° at 2 mm.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.43; H, 9.02.

In reductions conducted as above but at a temperature of 250° the yield of dialcohol never exceeded 40%. In one experiment carried out at 250° with catalyst 37KAF[8] the chief product had the composition of a **monohydroxy derivative of *o*-ethyl-*n*-propylbenzene,** b. p. 97–100° (2 mm.).

(8) Connor, Folkers and Adkins, THIS JOURNAL, **54**, 1138 (1932).

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.58; H, 9.86.

1-(β-Chloroethyl)-2-(γ-chloro-*n*-propyl)-benzene (IV).—Thionyl chloride (44.3 cc.) was added slowly (two drops per second) with stirring to 34.1 g. of the dialcohol at room temperature. Hydrogen chloride was evolved copiously and a reddish solution resulted. When the addition was complete the mixture was heated on the steam-bath for fifteen minutes, and then transferred with ether to a Claisen flask and heated on the steam-bath at the water pump vacuum until the excess reagent and sulfur dioxide had been removed (one and three-quarters hours). The dichloride distilling at 130–132° (2 mm.) as a colorless liquid weighed 39.6 g. (96%). In other runs yields of 89.5 and 94% were obtained.

Anal. Calcd. for $C_{11}H_{14}Cl_2$: Cl, 32.66. Found: Cl, 32.88.

1-(β-Cyanoethyl)-2-(γ-cyano-*n*-propyl)-benzene (V).—A mixture of 39.6 g. of the dichloride in 800 cc. of 95% alcohol and 47.5 g. of potassium cyanide in 100 cc. of water was refluxed for a total of twenty and one-half hours; the process was interrupted at one point for filtration from accumulated salt when this caused troublesome bumping. The alcohol was removed by distillation, the dark residue was extracted with ether and the product distilled at 2 mm. A fore-run (20.4 g.) distilled below 195°, and a fraction consisting of the dinitrile (13.5 g.) boiled at 195–210°, leaving 2 g. of residue. The fore-run was refluxed in 50 cc. of water and 250 cc. of alcohol with 24.5 g. of potassium cyanide for forty-two hours, and the resulting mixture afforded 5.6 g. of low-boiling material, 9.2 g. of dinitrile, b. p. 196–212° (2 mm.), and 4.9 g. of residue. The total yield of crude material was 63%. Analysis of a sample taken at 198° indicated the presence of a trace of chloride (Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 77.82; H, 6.87; N, 13.59).

Cyclization of the Dinitrile.—A solution of 18.3 g. of naphthalene in 415 cc. of dry ether was treated with 5.5 g. of sodium wire which had been cleansed in ether containing a little alcohol and rinsed in ether. The flask was fitted with a stirrer and condenser, the air was displaced with a slow stream of dry nitrogen, and 31.6 cc. of methylaniline was added. The mixture soon became yellow and after refluxing for one and one-half hours the sodium had completely disappeared. A Hershberg capillary dropping tube[9] was mounted at the top of the condenser, with the tip touching the condenser wall to promote an even flow of liquid, and charged with a solution of 16.6 g. of the crude dinitrile in 250 cc. of ether. The solution was added in the course of one and one-quarter hours with vigorous stirring and refluxing. A white solid formed as the reaction proceeded. Refluxing was continued for thirty minutes after the last of the dinitrile had been added and, after cooling, water was added slowly with stirring and the aqueous layer was discarded. The ether layer was concentrated and the residual orange oil steam distilled to remove methylaniline and hydronaphthalenes. The residue was a light brown oil which solidified easily and which afforded on crystallization from alcohol 11.9 g. (71%) of colorless, coarse needles,

(9) Hershberg, "Organic Syntheses," Vol. 18, 1938, p. 16.

m. p. 121–142°. On further crystallization of this mixture from alcohol, the less soluble **A-isomer, 1-cyano-2-iminobenzocycloöctane (VI)**, was easily obtained in a pure form consisting of coarse needles, m. p. 146–147.5°.

Anal. Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; molecular weight, 198. Found: C, 78.94; H, 7.01; molecular weight (micro-Rast), 195.

The more soluble B-isomer could not be isolated in a pure condition; the best sample formed heavy needles, m. p. 124–126°. Examination of the more readily separated keto-nitrile mixture indicated that the crude cyclization product contained 72% of the A-isomer. There was little change in the total yield of imino-nitrile mixture when the dinitrile was added much more rapidly. Thus the yield of the A-isomer, determined after hydrolysis, was the same as above with an addition period of eighteen minutes and in a 1-g. run fell off by less than 10% on adding the dinitrile in twenty-five seconds.

Conversion to the Keto Nitriles. A-Isomer (2-Cyanobenzocycloöctanone-3, IX).—The A-iminonitrile (5.24 g.) dissolved readily in concentrated hydrochloric acid (20 cc.) and, when it was nearly all in solution, the keto nitrile rapidly separated. The suspension was warmed gently on the steam-bath, cooled, diluted with water, and the white product collected. Crystallization from alcohol gave 4.6 g. (87%) of needles, m. p. 146–147.5°, in two crops. Recrystallization did not change the melting point.

Anal. Calcd. for $C_{13}H_{13}ON$: N, 7.03. Found: N, 6.83.

The substance dissolves readily in 1 *N* sodium hydroxide and was recovered unchanged (m. p. 146–147.5°) after the solution had been boiled.

Hydrogenation of the A-keto nitrile in acetic anhydride solution in the presence of Adams catalyst gave a substance having the composition of **2-acetylaminomethylbenzocycloöctanone-3.** This crystallized from dilute alcohol in clusters of needles, m. p. 153.5–154.5°. Attempted reduction of the carbonyl group by the Clemmensen method gave an unpromising oil.

Anal. Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81. Found: C, 73.82; H, 7.81.

The **B-isomer (probably 4-cyanobenzocycloöctanone-3, X)** was prepared by hydrolyzing the mixture of iminonitriles as described for the A-isomer and fractionally crystallizing the product from ether. The use of alcohol as solvent led to the formation of high melting material, and since this was not noted with the pure A-compound, it presumably arises from the other isomer present. The more soluble B-isomer is separated only with difficulty using ether. A small sample was obtained as colorless blades melting constantly at 96.5–97.5°; the major portion melted at 84–88° but gave satisfactory keto amide on hydrolysis.

Anal. Calcd. for $C_{13}H_{13}ON$: C, 78.36; H, 6.58. Found: C, 78.69; H, 6.61.

The substance gives a crystalline, water soluble sodium salt and can be recovered unchanged (m. p. 96–97°) from an alkaline solution.

The Keto Amides.—The **A-isomer** was prepared by dissolving 1.0 g. of the A-keto nitrile in 2.5 cc. of a mixture of 2.35 cc. of water and 7.65 cc. of concentrated sulfuric acid by warming and heating the solution on the steam-bath for five minutes. The solution was chilled and diluted slowly with water until no more oil precipitated. The oil solidified on being moistened with ether, and the solid was collected, ground in a mortar, and washed free of acid. The dried material weighed 0.9 g. (82.5%), m. p. 127–130°. Crystallization from alcohol–water gave white prisms which sintered at 129° and melted at 130–131°.

The **B-isomer** was obtained similarly from the pure B-keto nitrile (77 mg., m. p. 96–97.2°) in 96.5% yield (m. p. 224–230°). Purified from alcohol, in which it is sparingly soluble, the substance formed colorless needles, m. p. 239–241.5°, dec. A less pure starting product (m. p. 85–88°) gave crude amide, m. p. 228–234°, in 88% yield.

Anal. Calcd. for $C_{13}H_{15}O_2N$: C, 71.86; H, 6.96. Found: (A) C, 71.88; H, 7.01. (B) C, 71.79; H, 6.99.

The Hydroxy Amides.—For hydrogenation 0.9 g. of the A-keto amide in 9 cc. of alcohol was shaken with hydrogen in the presence of 50 mg. of Adams catalyst for about one hour, when absorption was complete and the product was found to have separated in a crystalline condition. The total material collected amounted to 0.82 g. (90%), m. p. 180–182.5°. The analytical sample of the A-isomer crystallized from alcohol in needles, m. p. 181.5–182.5°. The crude amide can be used for the reaction but must be completely free from acid or the yield is very poor.

The **B-isomer** was obtained by shaking a suspension of 0.5 g. of the amide in 7 cc. of alcohol with 50 mg. of Adams catalyst and hydrogen for one and one-half hours, when the theoretical amount of gas had been absorbed and the solid had gone into solution. The product was obtained from the filtered and concentrated solution by dilution with water in quantitative yield. The purified substance crystallized from alcohol–water as needles, m. p. 157.5–160°.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.20; H, 7.82. Found: (A) C, 71.23; H, 7.84. (B) C, 71.35; H, 7.68.

A-Hydroxy Acid (XIV).—The hydroxy amide (50 mg.) was brought into solution in a mixture of 1 cc. of hydroiodic acid (sp. gr. 1.7) and 0.6 cc. of water by warming, a little red phosphorus was added and the solution refluxed for two hours. An oil began to separate after the first hour, and after cooling this was removed in a semisolid state. A part of the material dissolved in 1 *N* sodium hydroxide and on acidification of the alkaline extract a solid separated. Crystallization from dilute alcohol gave 10 mg. of white needles, m. p. 132–134°. The substance dissolves in cold bicarbonate solution.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.73; H, 7.76.

The hydroxy acid was also obtained in about the same yield by hydrolysis of the hydroxy amide with 6 *N* hydrochloric acid; with isoamyl nitrite and acetic acid the yield was lower.

Δ^2(?)-Benzocycloöctene-2-carboxylic Acid (A-Series, XV).—A solution of 596 mg. of the hydroxy amide in 5 cc. of hydriodic acid (sp. gr. 1.7) was refluxed for thirty-five minutes, the separation of oil commencing after about ten minutes. After cooling, the hardened oil was removed, washed and dried, and boiled for five minutes with a little quinoline. The quinoline was extracted with very dilute acid and the semicrystalline residue was crystallized from

dilute alcohol, giving 105 mg., m. p. 115–130°. Further purification gave 78 mg. of material which melted at 128–137° and gave no depression when mixed with a purer specimen obtained in another experiment. This formed colorless needles, m. p. 140–140.5°.

Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.41; H, 7.25.

Benzocycloöctane-2-carboxylic Acid (A-Series, XVI).—A solution of 78 mg. of the crude unsaturated acid in 2 cc. of alcohol was hydrogenated in the presence of 15 mg. of Adams catalyst. The material collected from the filtered solution partially crystallized on contact with dilute alcohol, but purification with solvents was not practical. A suitable method was found in suspending the semisolid material in water, heating, and adding dilute sodium bicarbonate solution carefully until the crystals had all dissolved and the accompanying oil began to dissolve. The cooled aqueous solution was then extracted many times with ether and acidified, when 44 mg. of solid acid precipitated. In this condition the substance could be purified from petroleum ether (30–60°) and was obtained as clusters of colorless blades, m. p. 78.5–80°, with slight sintering at 77°.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.49; H, 8.15.

Benzocycloöctanone-3 (XII). A-Series.—The A-keto-nitrile (2.5 g.) was dissolved by warming in a mixture of 7.65 cc. of concentrated sulfuric acid and 2.35 cc. of water and the solution was heated for five minutes on the steam-bath, cooled, diluted with 10 cc. of water, and refluxed for fifteen minutes. Carbon dioxide was evolved and an oil separated. After cooling and diluting with water, the mixture was extracted exhaustively with ether and the extract was washed with ammonium hydroxide, dried and evaporated. The residue crystallized readily, giving 2.09 g. (95.5%) of ketone, m. p. 47–49°. Ordinary solvents seemed unsatisfactory for recrystallization and the best results were obtained by dissolving the substance in pyridine and slowly diluting with water. This gave colorless needles, m. p. 47.5–49°. The ketone distills readily with steam and a sample so purified melted at 48.5–50.5°. Because of its volatility the ketone should be kept in a stoppered vial.

Anal. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.67; H, 8.47.

The **oxime** was prepared by refluxing for two hours a solution of 0.42 g. of the ketone in 4 cc. of alcohol with 0.5 g. of hydroxylamine hydrochloride and 0.5 cc. of pyridine. On evaporating the alcohol and adding water, the product separated as an oil which soon solidified (0.43 g.). The substance crystallized from dilute alcohol in clusters of blades, m. p. 112.5–114°.

Anal. Calcd. for $C_{12}H_{15}ON$: C, 76.15; H, 7.99. Found: C, 76.33; H, 7.82.

When a solution of benzocycloöctanone and nitromethane in pyridine was allowed to stand overnight at room temperature there was produced a **compound** which appears to contain two nitromethane residues. The substance formed beautiful needles from alcohol, m. p. 106–107°.

Anal. Calcd. for $C_{14}H_{18}O_4N_2$: C, 60.42; H, 6.52. Found: C, 60.49; H, 6.61.

From the B-Keto Nitrile.—Acid hydrolysis of 50 mg. of the B-compound, m. p. 96.5–97.5°, was conducted as described for the isomer, giving 37 mg. (84.5%) of ketone which melted at 47.5–50.5° and showed no depression when mixed with the sample from the A-isomer.

Benzocycloöctanol-3.—A mixture of 2.85 g. of benzocycloöctanone-3, 5 cc. of alcohol, and 0.5 g. of catalyst 39KAF[8] was hydrogenated at 200° and an initial pressure of 2330 lb. (about two and one-half hours). The collected product distilled at 123–129° (2 mm.) and solidified when moistened with petroleum ether. The crude material (2.58 g., m. p. 55–58°) was crystallized from petroleum ether, in which it is sparingly soluble, giving 2.28 g. (79%) of alcohol, m. p. 62–64°. Further crystallization raised the melting point to 63–65°.

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 82.09; H, 9.33.

The yield was very low when the hydrogenation was conducted with Adams catalyst at room temperature. When heated with palladium charcoal the alcohol was converted in about 50% yield into benzocycloöctanone-3.

Benzocycloöctane-3-carboxylic Acid (XIII).—A solution of 0.33 cc. of phosphorus tribromide in 1 cc. of chloroform was dropped slowly into a solution of 1.2 g. of benzocycloöctanol-3 in 2 cc. of chloroform maintained at a temperature of −8 to −5°. The reaction tube was then stoppered with a calcium chloride tube and kept at −8 to −3° for five hours, at 5° for ten hours, and at room temperature for ten and one-half hours. The solvent was then evaporated and the residual oil heated on the steam-bath for seventy minutes. After adding ice, the bromide was extracted with ether. The solution was washed with water and with dilute alkali, which acquired an orange color, dried and evaporated. The bromide distilled at 125–133° (2 mm.) as a colorless oil; although the bromine content was 2.7% below that calculated, the material proved satisfactory for use; yield 0.86 g. (52%).

A solution of 0.86 g. of the crude bromide in 5 cc. of ether containing a trace of ethylmagnesium bromide was treated with 0.1 g. of magnesium, and after warming and manipulation of the metal the reaction started and was complete in two hours. The solution was chilled to −70°, a piece of dry-ice was added, and the mixture was allowed to warm slowly and then to stand at room temperature. After acid hydrolysis and extraction with ether, the acid was extracted with bicarbonate solution and obtained as a solid on acidification of the aqueous solution. The crude acid weighed 0.22 g., m. p. 120–137°. It was purified from dilute alcohol, crystallizing in clumps of colorless needles melting at 142–144° (slight sintering at 139°).

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.64; H, 8.06.

Summary

Benzocycloöctanone-3, required as an intermediate for the synthesis of benzocycloöctatetraene, can be obtained conveniently in 17% yield in an eight-step synthesis starting with the

known reductive cleavage of 2-hydroxy-3-naphthoic acid to *o*-phenylene acetic propionic acid. This is converted to a dinitrile which is cyclized by the Ziegler process; the resulting isomeric imino nitriles, whose probable structures are indicated by certain transformations, both yield benzocycloöctanone-3 on exhaustive acid hydrolysis.

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The Preparation of Aromatic Oxazolidines

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The establishment of aminophenyl oxazolines as local anesthetics[1] leads to the belief that compounds of closely related structure might possess interesting physiological properties. Some of these related compounds have already been studied, mainly by Adams and his co-workers.[2] These include the aminophenyl pentoxazolines, the aminophenyl thiazolines and thiazines and the aminophenyl oxazoles and thiazoles. The aminophenyl oxazolidines have not been similarly investigated. Such a study should be of interest. port upon the physiological possibilities of the aminophenyl derivatives will follow at a later date.

In the course of this work, it was found that *o*-chlorobenzaldehyde and salicylic aldehyde yielded only addition compounds. This may be due to the existence of these compounds in a chelated form. All other aldehydes investigated proceeded to the oxazolidine stage by dehydration.

The oxazolidines are in general yellow, or slightly yellow, liquids or solids of a basic nature, easily hydrolyzed by water or alcohol. They are insoluble (or hydrolyzed) in water; soluble in benzene and chloroform. Due to hydrolysis, positive reactions for monoethanolamine and the aldehydes are obtained with bromine water, potassium permanganate, silver nitrate and Schiff reagent. Hydrolysis also accounts for the fact that the oxazolidines yield, in general, the picrate of monoethanolamine and the phenylhydrazone of the aldehyde.

TABLE I

OXAZOLIDINES

Oxazolidine	Color	B. p. °C.	Mm.	M. p., °C.	Mol. formula	Nitrogen analyses, % Theory	Found
2-Phenyl	Yellow	157	(24 mm.)		$C_9H_{11}ON$	9.39	9.56
2-(*m*-Tolyl)-	Yellow	159	(14 mm.)		$C_{10}H_{13}ON$	8.58	8.71
2-(*p*-Tolyl)-	Yellow	153	(15 mm.)		$C_{10}H_{13}ON$	8.58	8.78
2-(*o*-Methoxyphenyl)-	Yellow	195	(27 mm.)		$C_{10}H_{13}O_2N$	7.81	7.87
2-(*p*-Methoxyphenyl)-	Yellow	180	(12 mm.)		$C_{10}H_{13}O_2N$	7.81	7.87
2-(*p*-Hydroxyphenyl)-	Cream			169	$C_9H_{11}O_2N$	8.48	8.56
2-(*m*-Nitrophenyl)-	White			73	$C_9H_{10}O_3N_2$	14.28	14.12
2-(*o*-Nitrophenyl)-	White			58	$C_9H_{10}O_3N_2$	14.28	14.22
ADDITION COMPOUNDS							
From							
Salicylic aldehyde	Yellow	180	(13 mm.)		$C_9H_{13}O_3N$	7.64	7.50
o-Chlorobenzaldehyde	Yellow	178	(22 mm.)		$C_9H_{12}O_2NCl$	7.00	7.04

While much work is reported in the literature dealing with the preparation of aliphatic oxazolidines, there is surprisingly little on the aromatic analogs, the only compound of this type reported being phenyl oxazolidine.[3] The method of preparation for the latter was found impractical in attempting to synthesize others of the aromatic series. This paper deals with an improved method for preparing substituted phenyl oxazolidines and reports the synthesis of seven new ones. A re-

(1) M. T. Leffler and Roger Adams, THIS JOURNAL, **59**, 2252 (1937).

(2) A. Novelli and Roger Adams, *ibid.*, **59**, 2259 (1937); S. H. Babcock and Roger Adams, *ibid.*, **59**, 2260 (1937); B. S. Friedman, Meredith Sparks and Roger Adams, *ibid.*, **59**, 2262 (1937).

(3) L. Knorr and H. Matthes, *Ber.*, **34**, 3487 (1901).

Experimental

p-Hydroxyphenyl oxazolidine.—*p*-Hydroxybenzaldehyde was dissolved in butanol and an equivalent quantity of